Figure 1

Human Nrg-ICD Polypeptide Sequence

SEQ ID NO: 1

KTKKQRKKLHDRLRQSLRSERNNVMNMANGPHHPNPPPDNVQLVNQYVSKNIIS
SERVVERETETSFSTSHYTSTTHHSMTVTQTPSHSWSNGHTESILSESHSVLVSSSV
ENSRHTSPTGPRGRLNGIGGPREGNSFLRHARETPDSYRDSPH
SERYVSAMTTPARMSPVDFHTPTSPKSPPSEMSPPVSSLTISIPSVAVSPFMDEERP
LLLVTPPRLREKYDNHLQQFNSFHNNPTHESNSLPPSPLRIVEDEEYETTQEYEPA
QEPPKKLTNSRRVKRTKPNGHISSRVEVDSDTSSQSTSSESETEDERTGEDTPFLSI
QNPMATSLEPAAAYRLAENRTNPANRFSTPEELQARLSSVIANQDPIAV

Figure 2

/gene="Nrg1" /note="IG; Region: Immunoglobulin" /db_xref="CDD:smart00409" misc_feature 1038..2222 /gene="Nrg1" /note="Neuregulin; Region: Neuregulin family" /db_xref="CDD:pfam02158" 900 a 867 c 743 g 762 t BASE COUNT **ORIGIN** 1 gcggccgcag ctgccgggag atgcgagcgc agaccggatt gtgatcacct ttccctcttc 61 gggctgtaag agagcgagac aagccaccga agcgaggcca ctccagagcc ggcagcggag 121 ggacccggga cactagagca gctccgagcc actccagact gagcggacgc tccaggtgat 181 cgagtccacg ctgcttcctg caggcgacag gcgacgcctc ccgagcagcc cggccactgg 241 ctcttcccct cctgggacaa acttttctgc aagcccttgg accaaacttg tcgcgcgtca 301 ccgtcaccca accgggtccg cgtagagcgc tcatcttcgg cgagatgtct gagcgcaaag 361 aaggcagagg caaggggaag ggcaagaaga aggaccgggg atcccgcggg aagcccgggc 421 ccgccgaggg cgacccgagc ccagcactgc ctcccagatt gaaagaaatg aagagccagg 481 agtcagctgc aggctccaag ctagtgctcc ggtgcgaaac cagctccgag tactcctcac 541 tcagattcaa atggttcaag aatgggaacg agctgaaccg caaaaataaa ccagaaaaca 601 tcaagataca gaagaagcca gggaagtcag agcttcgaat taacaaagca tccctggctg 661 actctggaga gtatatgtgc aaagtgatca gcaagttagg aaatgacagt gcctctgcca 721 acateaceat tgttgagtea aacgagttea teactggeat gecageeteg actgagaeag 781 cctatgtgtc ctcagagtct cccattagaa tctcagtttc aacagaaggc gcaaacactt 841 cttcatccac atcaacatcc acgactggga ccagccatct cataaagtgt gcggagaagg 901 agaaaacttt ctgtgtgaat gggggcgagt gcttcacggt gaaggacctg tcaaacccgt 961 caagatactt gtgcaagtgc ccaaatgagt ttactggtga tcgttgccaa aactacgtaa 1021 tggccagctt ctacaaagcg gaggaactct accagaagag ggtgctgaca attactggca 1081 tctgtatcgc cctgctggtg gtcggcatca tgtgtgtggt ggcctactgc aaaaccaaga 1141 agcagcggca gaagcttcat gatcggcttc ggcagagtct tcggtcagaa cggagcaacc 1201 tggtgaacat agcgaatggg cctcaccacc caaacccacc gccagagaac gtgcagctgg 1261 tgaatcaata cgtatctaaa aacgtcatct ccagtgagca tattgttgag agagaagtgg 1321 agacttcctt ttccaccagt cattacactt ccacagccca tcactccacg actgtcaccc 1381 agactectag teacagetgg agtaatggge acaeggagag egteatttea gaaageaact 1441 ccgtaatcat gatgtcttcg gtagagaaca gcaggcacag cagtcccgcc gggggcccac 1501 gaggacgtct tcatggcctg ggaggccctc gtgataacag cttcctcagg catgccagag

1561 aaacccctga ctcctacaga gactctcctc atagcgaaag gtatgtatca gccatgacca

1621 ccccggctcg tatgtcacct gtagatttcc acacgccaag ctcccctaaa tcgccccctt 1681 cggaaatgtc tccacccgtg tccagcatga cggtgtccat gccctctgtg gcagtcagcc 1741 cctttgtgga agaagagagg cctctgctgc ttgtgacgcc accaaggcta cgggagaaga 1801 aatatgatca tcaccccag caactcaact cctttcatca caaccctgca catcagagta 1861 ccagcctccc ccctagccca ctgaggatag tggaggatga ggagtacgag acgacccagg 1921 agtatgagtc agttcaagag cccgttaaga aagtcaccaa tagccggcgg gccaaaagaa 1981 ccaagcccaa tggccacatt gccaataggt tggaaatgga cagcaacaca agttctgtga 2041 gcagtaactc agaaagtgag acagaagacg aaagagtagg tgaagacaca ccattcctgg 2101 gcatacagaa ccccctggca gccagccttg aggtggcccc tgccttccgt ctggctgaga 2161 gcaggactaa cccagcaggc cgcttctcca cacaggagga attacaggcc aggctgtcta 2221 gtgtaatcgc taaccaagac cctattgctg tataaaacct aaataaacac atagattcac 2341 tttagcagtt ctgcaaatag aaaacaggaa gaaaaaaaaa cttttataaa ttaaatatat 2401 gtatgtaaaa atgtgttatg tgccatatgt agcaattttt ttacagtatt tcaaaaacga 2461 gaaagatatc aatggtgcct ttatgttctg ttatgtcgag agcaagtttt ataaagttat 2521 ggtgatttct ttttcacagt atttcagcaa aacctcccat atattcagtt tctgctggct 2581 ttttgtgcat tgcattatga tgttgactgg atgtatggtt tgcaaggcta gcagctcgct 2701 ctctctctct ctctctctct ctctctctct ctctctctct ctctgtctct 2761 cccgtagctc ccaaccagta ctgtcttgga ctggcacatc catccaaata cctttctact 2821 ttgtatgaag ttttctttgc tttcccaata tgaaatgagt tctctctact ctgtcagcca 2881 aaggtttget teaetggact etgagataat agtagaceca geageatget aetattaegt 2941 atagcaggaa actgcaccaa gtaatgtcca ataataggaa gaaagtaata ctgtgattta 3001 aaaaaaaaa caaactatat tattaatcag aagacagctt gctcttggta aaaggagcta 3061 ccattgactc taattitgac tttttagtta ttgttcttga caaagagtaa cagcttcaag 3121 tacagectag aaaaaaaaat gggttetgge etgetateag gataaateta tegaegtaga 3181 tagattcaac tcagtttcac tttctgtctt gggggaaatg atccagccac tcatatgacg 3241 accaaccaac cacaggtgcc tctgctccct gt

Figure 3

Nuclear localization sequences

SEQ ID NO: 3

KTKKQRKK

SEQ ID NO: 4

PRLREKK

Figure 4

Binding sites in Nrg-ICD for Eos

SEQ ID NO: 5

KTKKQRKKLH

DRLRQSLRSE

RNNVMNMANG

PHHPNPPPDN VQLVNQYV

SEQ ID NO: 6

SERYVSAMTTPARMSPVDFHTPTSPKSPPSEMSPPVSSLTISIPSVAVSPFM DEERPLLLVTPPRLREKYDNHLQQFNSFHNNPTHESNSLPPSPLRIVEDEEYETTQ EYEPAQEPPKKLTNSRRVKRTKPNGHISSRVEVDSDTSSQSTSSESETEDERTGED TPFLSIQNPMATSLEPAAAYRLAENRTNPANRFSTPEELQARLSSVIANQDPIAV

Figure 5

Human Eos binding domain for DNA

SEQ ID NO: 7

LKCDVCGMVCIGPNVLMVHKRSHTGERPFHCNQCGASFTQKGNLLR HIKLHSGEKPFKCPFCNYACRRDALTGHLRTHSVSSPTVGKPYKCNY CGRSYKQQSTLEEHKERCHNYL

Figure 6

Human Eos binding domain for Nrg-ICD

SEQ ID NO: 8

 $\hbox{\tt CEHCRILFLDHVMFTIHMGCHGFRDPFECNICGYHSQDRYEFSSHIVRG} \\ \hbox{\tt EHKVG}$

Figure 7

Peptides that block Nrg-ICD/Eos signaling

SEQ ID NO: 9 YGRKKRRQRRR CEHCRILFLDHVMFTIHMGCHGFRDPFECNICGYHSQDRYEFSSHIVRGEHKVG

SEQ ID NO: 10 RQIKIWFQNRRMKWKK CEHCRILFLDHVMFTIHMGCHGFRDPFECNICGYHSQDRYEFSSHIVRGEHKVG

SEQ ID NO: 11 DAATATRGRSAASRPTERPRAPARSASRPRRPVE CEHCRILFLDHVMFTIHMGCHGFRDPFECNICGYHSQDRYEFSSHIVRGEHKVG